

JACOBI (A.)

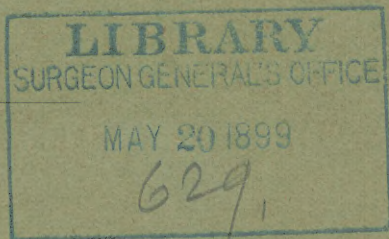
ERGOT IN CHRONIC MALARIA.

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THESE notes are written exclusively for clinical purposes. That is why a few words on the active principles of ergot may suffice. They are sphacelinic acid, cornutin, also trimethylamin, vernin, and ergotinic acid. Trimethylamin gives rise to cerebral spasms which may become tetanic. It increases reflex irritability, and according to Gaethgens, accelerates, by irritation of centers located in the medulla oblongata, respiration and blood-pressure. Vernin, which was found by Schulze and Bosshard, is a new xanthin substance with effects similar to those described above. Sphacelinic acid (spasmo-toxin, sphacelo oxin) so called by Kobert who first studied and named it, when absorbed in the intestine causes a hyaline degeneration of the blood-vessel walls, which first contract and finally dilate, also coagulation inside the vessels with consecutive gangrene. In proportion to the doses taken it causes paresthesia, alopecia, falling out of the nails, and gangrene of the skin or of the extremities. Fortunately, it is easily decomposed, so speedily indeed that ergot a year old contains none at all. The effective principle is cornutin, found and named by Kobert. What Tanret called ergotinin is chemically

¹ Read at the Annual Meeting of the American Climatological Association at Bethlehem, N. H., September 1, 1898.

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identical with it, but does not equal it in efficiency when prepared according to Kobert. It is easily decomposed when exposed to light or air. There is but little of it in ergot, all the alkaloids forming but 0.2 per cent. of the drug. It irritates the medulla oblongata, contracts arteries, increases blood-pressure, and contracts the unstriated muscular fiber in general. It is employed as a citrate or a chlorid. Kobert speaks of it as enclosed in capillaries holding 0.005 for subcutaneous use, or in pills of 0.002. In Merck's index, "cornutin" and "cornutin citrate" are enumerated. In poisonous doses it causes convulsions and contractures, also toxic polyneuritis, such as follows overdoses of arsenic, lead, phosphorus, alcohol, or mercury. Ergotinic acid, called sclerotinic acid in its impurer state, lowers the blood-pressure in animals. Before knowing better, I recommended it even in my "Therapeutics" for subcutaneous injections to obtain the effect of ergot; that was a serious mistake. In the intestinal tract it is decomposed, and under the skin it is painful and irritating.

All of these constituents lose their power while in the ergot, from month to month. It should be gathered before the rye is perfectly ripe for harvesting, but generally is not. The decomposition of the grain is mainly due to its large percentage (39) of fat; that is why a salutary effect is often missed and the opinions in regard to the efficiency of the drug differ. The effect of the extract or fluid extract depends on the retention of the cornutin. All such preparations as are deprived of the substances soluble in alcohol, are deteriorated thereby, for it is the

active alkaloids that are soluble in alcohol. In the fluid extracts the alcohol should be strong enough to hold the alkaloids and dilute enough to dissolve but little of the fat. As far as I am concerned, I have employed for internal use, whenever possible, the solid alcoholic extract of the pharmacopoeia. It seemed to me to give better results than even Bonjean's ergotin, which has been in the market since 1842. At all events, the value of ergot preparations is in their undecomposed alkaloids; everything else is either indifferent, disturbing, or injurious.¹

The effect of ergot and its preparations, when given in medicinal doses, is mainly spent on the unstriped muscular fibers. Its effect on the uterus has been known and used and abused a long time. The muscles of the vagina were found to be influenced by it by Swiecichi.² That is why I felt encouraged more than forty years ago to administer it in conditions of hyperemia and of the acute and subacute inflammations of such organs whose blood-vessels are not entirely or almost deprived of muscular layers. The media of small arteries has unstriped muscular fibers. There are several of these layers in the larger ones, which besides are supplied with elastic fibers. This structure is uniform in all the arteries of the body. The veins, however, exhibit more startling differences, nowhere more than in the tunica media. It consists of circular muscular fibers, elastic network and fibrillar connective tissue, is best developed in the v. poplitea and the other veins of the lower ex-

¹ Kobert, "Lehrb. d. Pharmako-Therapie," Stuttgart, 1897, p. 502.

² Quoted by Kobert, "Intoxicationen," p. 185, 1893.

tremities, less in those of the upper extremities, still less in those of the abdominal cavity. It is *absent*—and here is an important point—*from the veins of the pia and dura mater*, of the retina and the bones, the vena cava, and all the veins emanating from the capillaries, where the media consists of transverse and oblique bundles of connective tissue only.¹

As I said, the veins of the pia and dura have no muscular fiber in the media; moreover, in the cranial cavity they are long and distant from their arterial pressure-supply. That is why I am never surprised when the employment of ergot in brain disease is wholly futile. Circumstances are different in connection with the spinal canal. The veins of the cord and its membranes are no better supplied with contractile elements than those of the cranial cavity; but because of their shortness they are under the immediate influence of blood-pressure. That is why ergot, so useless in brain disease, is perfectly adapted to cases of spinal hyperemia, or to acute, or subacute spinal inflammation.²

¹ Ph. Stoehr "Histology," seventh edition, p. 91.

² In hemorrhages, such as those of the lungs, ergot has long been used by some with great confidence, by others with indifferent success. Among the latest preparations is ergotinol, of which 1 c. c. corresponds to a gram of extract of ergot, which Vosswinkel eulogizes highly in pulmonary hemorrhages when used subcutaneously. Some think highly of ergot in all sorts of inflammatory processes. There is Croq of Brussels, for instance, who employs it in tuberculosis. In his opinion the tendency of tuberculosis is rather that of getting well, unless complicated by inflammatory processes to counteract which no medication seems to be more indicated than that of ergot. Certain forms of spermatorrhea and nocturnal enuresis connected with muscular incompetency of the sphincter are frequently benefited. Here its effect may be the direct one on the unstriated fiber, or on the spinal center of the sphincters which must be taken to be present in the lumbar cord along the uterine and spermatic centers. It has been given in Graves' disease for the same reason, not to speak of, for reasons unintelligible to me, its use in non-pancreatic diabetes

The practice of employing ergot in spinal cases was gradually developed. In a report published in the *New York Medical Monthly*, during the years 1860 and 1861, on my clinic of the diseases of children in the New York Medical College, then in existence, you may find a few of my earlier cases in which I employed ergot for the purpose of contracting blood-vessels and relieving hyperemia and inflammation in spinal diseases.

Number 68 is a case of acute poliomyelitis; number 122, one of spinal meningitis; number 167, one of spinal hyperemia. So far as I know they are the first I published after some years of experience with the drug. In regard to the latter disease my information was obtained from a friend who at that time was stationed at the Emigrant Hospital of Ward's Island, Dr. Francis Simrock. Some histological considerations encouraged me besides in employing it in this way. The capsule of the spleen consists of dense and hard connective tissue, unstriped muscular fiber, and an elastic network. It sends off numerous processes, leaf- and string-like layers, into the interior of the spleen, thus forming a coherent network which contains the pulp. This network also contains, besides connective tissue, copious unstriped muscular fibers. Thus it seems there is no organ in the animal economy more

mellitus, sea-sickness, and whooping-cough. In the paralytic form of hemicrania it has been highly recommended, and may be all of us have employed it. In tabes, spastic spinal paralysis, in progressive bulbar paralysis, it has been used because of the supposition that the anatomical lesion is attended by dilatation of blood-vessels. The results are but few or none. At all events, no physiological effect can be expected except in the initial stages when there still is or may be spinal congestion.

amenable to the action of a muscle-contracting agent.

The employment of ergot in moderate doses has no dangers under most, ordinary circumstances. I have used it these forty years extensively, for weeks and even months in succession, without a single case of intoxication. The latter has frequently been observed in all countries of Europe, mostly in the past. If we hear of epidemics or endemics of ergotism, there are but few countries in which they are often met with, *viz.*, Spain, and still more, Russia. With the increase of civilized agriculture and a slight improvement in the general condition and nutrition of the population, the average of good rye increases, that of ergot decreases. In every harvest of corn there is some ergot; one per cent. is common and not attended with danger. But when a population is starved and subjected to malaria and other infectious diseases, and unclean and sleepless from hard work, starvation, and anxiety, and when they are fed on rye with a large percentage of ergot, and particularly when it is of recent growth, during and a very few months after cutting, ergotism may make its appearance.

There is danger in poisoning only, not in medication. In connection with malaria there are two organs we have to consider when medicating, the blood and the spleen, the former because it contains the sporozoa, the latter because of its sponge-like mass in which it harbors the infected blood and serves as a receptacle of dangers. It appears that a direct effect on the blood or on the plasmodia is not required for a cure, but that gradually the restoration of the

spleen to a fairly normal size, forcing the stagnating blood into a normal circulation with progressive elimination of the plasmodia is sufficient to open the gates to recovery. That is what I believe I have often done by giving ergot in malaria.

The uncertainty of the effect may also be due to the fact that most preparations of ergot contain both ergotinic acid, which lowers arterial pressure, and cornutin which contracts the arteries. All of this should impress us with the necessity of using the alkaloid cornutin when it is obtainable. Even this substance should be used with great care, for instance, in hemorrhage, which may be increased by heightened blood-pressure.

CASE I.—A Hungarian boy, aged five years, just arrived in the country, October 10, 1859. Had fever and ague, mostly quotidian attacks, at his home. On the ocean he was better, *viz.*, now and then he had a day without an attack. He was pale, waxy, with extensive hemic murmurs and with albumin in the copious and watery urine. His spleen extended nearly to the spina anterior superior. Had regular daily attacks with great prostration, in spite of quinin and Fowler's solution. Of the former he took from 6 to 12 grains daily. Being previously constipated his bowels had been attended to. Not being acquainted with the fluid extract—perhaps it was not even in the market¹—I gave him an infuso-decoction, prepared with sulphuric acid, of half an ounce of ergot in 10 ounces of water, of which he was to take one-half tablespoonful three times a day. There being no improvement he took, after four days, the

¹ Dr. E. R. Squibb, in a letter dated September 21st, has kindly informed me that it was first prepared by Professor Wm. Procter, Jr., of Philadelphia in 1857 ("Proc. Amer. Pharm. Asso. for 1857," p. 130, and 1859, p. 271), and by himself since 1859.

same dose five times a day. When I saw him ten days later he had been without an attack three days. The doses were continued five days, then for five more days four daily doses were given, and thereafter but three. During all this time he had no attacks of fever, albumin became less, but his spleen was still as large as before under percussion and palpation. Finally he was removed from South Brooklyn where Gowanus Bay was as pestiferous at that time as the shores of the River Theiss, and gradually with the use of iodid of potassium, iodid of iron, and the occasional resumption of ergot, he improved. After a year I saw him again, looking well but pale, with no albuminuria, hardly any murmur, but his spleen still palpable 3 centimeters below the border of the ribs.

CASE II.—His brother, sixteen years old, gave me a new experience. He had the very same symptoms exhibited by his brother—hydremia, tumor of the spleen, etc., without albuminuria and without the history of chills. For the latter reason he had taken no medicine whatsoever. After purging him gently I ordered the same medicine to be taken in table-spoon-doses four times daily. Two days after beginning his treatment he had a very violent chill followed by perspiration; no temperature was taken, as he was miles away. He had another violent attack the next day, a milder one a few days after this, and then no more. He was treated like his brother, with the same slow but finally satisfactory result.

CASE III. — A. W., male, fourteen months old. Was seen by me October 1, 1880. Was breastfed until half a year previously, then fed on mixed food. Had diarrhea in the summer, and fell ill with pneumonia of the right side a fortnight before I saw him. This was watched carefully; I found but few remnants of it. But in the beginning of the second week the baby was taken with a convulsion, high

fever and vomiting, lips and fingers were bluish. After a few hours the condition improved, but on the following day, blue nails, high temperature, followed by apyrexia, and great debility were noticed. No return of pneumonia; no nephritis. Quinin was given in repeated doses for several days. No convulsion returned, but there were temperatures up to 102° and as low as 97° F. every day. The urine was pale all the time; more was passed during the high temperature, none during apyrexia. On October 1st this condition, of somewhat elevated temperature every day, which lasted a few hours, continued in spite of from 30 to 40 cg. of sulphate of quinin. There was no apparent reason for changing the medication, but care was taken to give the quinin doses during apyrexia and not within the last three hours before the expected attack. Up to October 5th there was hardly any change in the daily recurrence of temperature. The spleen became palpable and appeared sensitive on pressure; meanwhile no anomaly of heart, lungs, or kidneys. Quinin was then stopped, and fluid extract of ergot given in six, after five days, in five, after ten days, in four, daily doses of 10 minims each. On and after October 7th, no attack of fever; on the 10th the spleen could no longer be felt. Ergot was continued to November 15th, and Fowler's solution and syrup of the iodid of iron were given from October 15th to the end of the year.

CASE IV.—Mrs. M., thirty-one years old. In moderate health until the summer of 1890, though she lived in East 117th street, New York, a hot-bed of malaria even at the present time, until August when she moved to Brooklyn. The only exception to her average health consisted in neuralgic pains of uncertain duration, and at irregular intervals. Left hemicrania she had had for years, neuralgia of the left upper extremity during the summer; and for several weeks before she presented herself on November 24,

1890, neuralgia of the right lower extremity, posteriorly. This pain grew worse from slight pressure; deep pressure would diminish it. She had an extensive and loud systolic, a mild diastolic murmur, no enlargement of the heart, pale lips and conjunctivæ, and a small pulse of eighty. She had suffered from chills and fever since September; the tertian type had changed into the quotidian after a week; later she had two attacks a day. They would intermit now and then after heavy doses of medicine. During the previous fortnight she had taken 400 grains of quinin, and had almost daily attacks; she had a chill with a temperature of 104.4° F. in my office. Her spleen was 15 cm. long, 8 cm. wide, and sensitive over such of its surface as could be palpated. She was ordered to go to bed for at least a week, and to take 0.5 of calomel; at the same time a teaspoonful of Squibb's fluid extract of ergot four times a day in whisky and water. When after three days her chills continued, the dose was given six times a day, and no chill occurred after the fifth day until she presented herself on December 3d, nine days after her first call. Her spleen was 3 cm. shorter and less sensitive. She then was ordered 0.75 of sulphate of quinin once every fifth day in the forenoon, and the ergot was continued in the same doses. On December 7th she had a slight chill while still in bed in the morning. On December 10th, the ergot was reduced to 15 c.cm. a day, in four doses; on the 20th to 10 c.cm. On that day her spleen could still be felt slightly below the ribs. The quinin was continued to about the middle of January, the ergot another month afterward. At the same time, from December 20th to the end of January, she was given iodid of potassium, 5 grams, three times a day.

CASE V.—M. H., twenty-six years old. Was admitted November 11, 1897, and discharged December 6th. Was a moderate drinker and not venereal.

Had no previous sickness. After a two-weeks' sojourn in the South in September he had one morning a chill which lasted one-half hour, and was followed by perspiration. Such attacks he had every other day for two, then every day for three weeks. Quinin was taken and the type of his fever became tertian again. Lately, while he was still taking quinin,—mostly, he said, when the chill came on and enough to affect his hearing,—the type of his fever became mixed, sometimes every day, sometimes every other day, with a few intervals of some days. On the 11th of November his temperature was 100.4° F. at noon; a chill came on at 2 P.M., with a temperature of 103.2° and 104.4° F., which sank gradually. His spleen was quite tender on pressure below the ribs, and up in the seventh intercostal space, and was about 13 or 14 cm. long, as revealed by percussion. Plasmodia were found in large numbers. Squibb's fluid extract was given in four daily doses of a teaspoonful (4 c.cm.) each. The highest rectal temperature of November 12th was 100.8° F. at 2 P.M., of the 13th, 99.4° F., of the 15th, 99.2° F., 16th, 99.8° F. No chills. Did not feel quite well on the 20th, and was given a few teaspoonfuls of sodium sulphate. Highest temperature 99.6° F. at 8 P.M. Because of indigestion, with coated tongue, took sulphate of magnesium on the 21st. Temperature 101.2° F., but no chills. Spleen smaller, less sensitive, plasmodia still found occasionally. Highest temperature on the 22nd, 101.8° F., on the 23rd, 102.2° F., on the 24th, 101.8° F., on the 25th, 100° F., on the 26th, 99.8° F. During all these days he never had abnormal temperatures like those he exhibited while under the uncontrolled influence of his malaria; but normal they were not. Evidently the rise extending over days was due to an additional, probably, gastric influence. About this time plasmodia disappeared from his blood. He re-

mained under observation more than a week, and was then discharged.

CASE VI.—T. B., twenty eight years. Admitted May 10th. Had had syphilis nine years before, gonorrhea several times; was otherwise healthy with the exception of slight colds; drank "some." His feet had been swollen a little for seven months. During the previous three months had had chills and sweats, off and on, he said. Took a great deal of quinin, almost daily, which helped him. Temperature on admission 101.4° F., pulse 118, respiration 28; pallor, anemia. Sibilant and sonorous breathing over both lungs, anteriorly, breathing diminished over base of left lung posteriorly, with subcrepitant râles and dulness. Liver flatness from sixth rib downward to below the costal border; the organ was felt nine centimeters below it in the parasternal line. Spleen extended from the seventh rib in the axillary line to the crest of the ilium and to within 2½ centimeters of the median line. No edema, no ascites; kidneys negative; axillary lymph bodies slightly enlarged. Plasmodia found pigmented, flagellated, segmented. Fluid extract of ergot 4 c.cm. four times a day on and after the 12th of May, preceded by a dose of calomel and sodium bicarbonate on the 10th. May 15th: no chill since; no diminution of size of spleen, which feels a little softer. May 23rd, was up and about all the week; no paroxysm, spleen softer, no flagellated and no segmented plasmodia. Had no paroxysm to the end of the month; at that time no plasmodia, and spleen was less tense and shorter by almost three centimeters.

These cases are selected almost at random from my records; a great many were never recorded, since my experience with the drug was no longer doubtful. In connection with the subject I may here state that my success with ergot in chronic and

relapsing malaria encouraged me to try it in many cases of acute malarial infection. I am certain that many such cases will respond to the action of ergot, but in the average case less rapidly than to that of quinin. Indeed, these experiments were made for the sole purpose of observation.

CONCLUSIONS.

1. There are cases of chronic intermittent fevers with large tumefaction of the spleen, that after having resisted the action of quinin, arsenic, methylene blue, eucalyptus, and piperin are benefited by ergot.

2. When enlargement of the spleen is not old and not firmly established the contracting effect of ergot is noticed within a reasonable time.

3. The attacks will disappear before the diminution in the size of the spleen is very marked.

4. Though temperatures, after the employment of ergot, remain irregular and now and then somewhat elevated, chills, as a rule, are not noticed with this elevation.

5. Plasmodia do not seem to disappear from the blood so rapidly as they do after quinin, when the latter is effective. But even while some are still present, the attacks being more or less under control, the patient will feel better.

6. Complicating local pain requires additional treatment with ice, or cold douches, or heat; chronic hyperplasia demands iodid of potassium or iodid of iron. Digestive disorders may indicate, as they often do, when quinin is expected to act,

before the employment of ergot, an emetic, or a purgative, or stomachics.

7. An experience extending over forty years in which I have used ergot in many instances, justifies me in asserting at least this much: that there are many cases of chronic malaria, apparently intractable, that will get well with ergot.

8. There are cases, occasionally, in which the return of elevations of temperature after the successful use of ergot makes the combination of ergot and quinin, or ergot and arsenic advisable, though quinin and arsenic had not been successful previously.

9. Ergot, like quinin, probably by its sudden contracting effect on the spleen, and by the forcing of large quantities of plasmodia-laden blood into the circulation, is, in chronic malaria when hydremia and spleen tumor are excessive, capable of bringing on the very first attack of chills and fever.

10. Recent cases of malaria have got better, or were improved under the extensive use of ergot, but many resisted a long time; that is why acute cases should rather be treated with quinin.

DISCUSSION.

DR. BEVERLEY ROBINSON of New York said: If we look back I think we must all be of the opinion that probably blood-vessels in the different organs are affected; they seem to have a notable effect upon the malarial condition and, I should imagine, through the diminution of the size of the spleen in old malarial cases. The probability is that quinin does have some contracting influence on the spleen itself in addition to any particular effect it may have upon the blood. With that I can understand that

there is a rational view with regard to the action of ergot in its effect on the size of the spleen, and when the spleen comes to be contracted the malarial condition is fatally affected.

I would like to speak of something that I am extremely interested in, and hope some of the gentlemen present will be good enough to give their opinion. In a paper before the New York Academy of Medicine I called attention to the use of the tincture of bark in repeated doses and spoke of cases in which it had been notably useful. The cases were pretty closely observed in hospital wards and in my practice outside. If any of you have not read Huxham's original work on the treatment of fevers, and his remarks with reference to the treatment of malarial fever, I think you will be very much interested. It was published more than a hundred years ago and he gives the formula now used. He attributes a certain amount of merit to snakeroot. I believe we are getting away from facts which are of very great value. We are disposed to believe a little too much in using our alkaloids, because they are useful and are so easily administered. The bark itself is of very great benefit. I think there is a rational basis of belief that the bark itself will be of use in removing the poison of malaria. The bark must be given in many of these instances if one wishes to secure the best effects. I would refer to one preparation by a firm in the West, Parke, Davis, & Co. Compound fluid extract of cinchona is nothing more than the compound tincture of cinchona with five times its strength, so that if one gives 5 or 10 minims of the compound cinchona he is giving five times the strength of the tincture. I have found it a very useful way of giving the bark and have obtained very good effects from it.

DR. R. G. CURTIN of Philadelphia said that the treatment of malaria by ergot would be a valuable

addition to any specific treatment, by not only helping to keep down the size of the liver and spleen during the acute attack, but also by preventing the subsequent chronic enlargement of these organs.

DR. JUDSON DALAND of Philadelphia said: I have listened with great pleasure and profit to the remarks made by Dr. Jacobi in reference to the action of ergot in malaria, and I was especially interested in the observation regarding the influence of the drug on the spleen. In regard to those cases of malaria uninfluenced by quinin, so far as Philadelphia is concerned, we have very few cases that do not yield to the action of this drug. Along the Gulf States, more particularly in Louisiana, I am informed, a number of cases have occurred in which quinin has not exerted its usual beneficial effect.

One year ago while in Tiflis, at the Civil Hospital, Professor Gurko informed me that frequently they receive cases of malaria from the neighborhood of Batoum, on the Black Sea, which are influenced by large doses of the bichlorid of quinin administered by the mouth and hypodermatically. He stated that in the few months preceding he had treated in this way six cases. The cases had been accurately studied, the parasite had been pictured, and these pictures were shown me, and of the six cases five had resulted fatally. He also stated that many of these patients present symptoms of typhoid fever before the parasite is found in the blood, but other examinations have showed the affection to be malaria and not typhoid fever.

The use of quinin in malaria as we see it in Philadelphia sometimes fails to give results in cases unquestionably malarial, for several reasons. I recollect two such cases in the Philadelphia Hospital where the patients had malaria as demonstrated by the presence of the plasmodium in the blood. Quinin was given in sufficient quantity, but most of

it was recovered in the stool, and I have no doubt that in many cases of malaria the quinin is either insufficient primarily, or the pills are old and hard and only partially dissolved, or it is in capsules that are old and pass the pylorus and probably escape in the feces without the organism being impressed with this salt of cinchona. With the detection of the plasmodium of malaria, the number of cases of malaria in Philadelphia has rapidly decreased, until at the present time, except those cases coming from the Eastern Shore of Maryland and other malarial points, the disease is practically a rare one, and on an average in not one case in ten that are examined where the diagnosis of malaria has been made has it been verified by an examination of the blood.

Reference was made to the time of giving the drug, which is a matter of some importance, and it would seem as though, from what we now know of the disease, that the plasmodium is most exposed to the antidotal action of the quinin at the time when it has become the matured malarial body, floating free in the blood. It is quite evident that when the plasmodium is within the red blood-corpuscles quinin in solution in the plasma will not be able to exert its antiperiodic effect, but when the body breaks through the envelope of the red cell and enters the circulation quinin promptly destroys the parasite.

I would like to call attention to one case which unquestionably would have ranked a few years ago as a case of malaria. The patient had intermittent fever, occurring daily with the customary symptoms of the paroxysm. Examinations of the blood, urine, and viscera gave negative results. Examinations were repeated. The urine showed no change. The autopsy showed suppurative kidney with calculi impacted in the ureter. It would seem as though these calculi temporarily occluded the passage of

urine from the diseased kidney, but when the accumulation of urine became considerable, dilatation of the ureter took place, and partial escape of the contents occurred. The urine that upon examination gave negative results was probably secreted from the healthy kidney, while there was temporary obstruction of the left ureter. No distinct tumor could be found, although while examination was interfered with by the obesity of the patient, swelling was detected in the left renal region.

Regarding the action of ergot upon the essential poison of malaria, I doubt very much whether it has this effect. I personally have not had much experience in the use of this drug, for the reason just stated. As a rule, the disease as presented in Philadelphia yields to quinin. The poison that produces the paroxysm seems to be the result of the gradual maturing of the parasite of malaria, and at the moment of its maturity there seems to be thrown into the blood a chemical poison, this seeming to initiate the paroxysm, and I doubt whether ergot has any special influence over this low form of animal life.

DR. DIDAMA of Syracuse, N. Y., said: I live in a region which used to be swampy, and chills and fever were prevalent. Nearly forty years ago physicians treated the cases there by first giving something, such as calomel, to prepare the system to take the antidote of the poison. We knew nothing about bacteriology at that time. I could not see why we should not give an antidote at once, and so at that time I commenced giving that which I have been giving ever since. There was a tendency for the chills and fever to return in about seven or fourteen days. Then in order to prevent that return I thought I would repeat the medicine about every six or seven days, so I would give the patient ten or eleven powders, each one containing 4 to 5 or 6 grains of quinin with piperin and some sulphate of iron. I

have never varied the size of the dose from that day to this. The patients took the powders without any reference to what time of day the chill occurred. They took one in the morning and one in the afternoon or toward evening. A few of these powders were put up in blue papers, and the patient was to take one of these every Sunday morning for three or four Sundays. The men kept at work as usual, but there was no return of the disease that season. The next season they might have it again, and it was cured in the same way. I have had from 200 to 250 cases a year. Patients in Michigan took the same medicine with the same result. There were some cases which I did not see early enough. In those cases of chronic malarial poison with enlarged spleen this treatment does not act as well, and I am glad that Dr. Jacobi has told us what he has about the ergot in eliminating the poison from the spleen.

DR. JACOBI, in closing the discussion, said: There is no doubt that there are cases of malaria which do resist quinin, as there are cases that do resist arsenic, or quinin and arsenic together. I have seen them. If any man says he has not seen them (a great clinician whom I much admire rebukes those who do not succeed with quinin in every case), that is his luck and not mine. The spleen, of which we know almost nothing as yet, has certainly a great influence in harboring germs and in being the cause of the relapses not only in malaria, but in other diseases. I remind you of what we can all see in typhoid fever. I know that in a case of typhoid fever in which on the sixteenth or seventeenth day the spleen does not diminish in size there will be a relapse, or rather a continuance of the illness. In those cases in which the spleen diminishes in size about the sixteenth or seventeenth day, one is fairly certain that with the usual care there will be no re-

lapse. That is one of the instances of which I can feel tolerably sure as a matter of experience, which is, that the spleen certainly has a great deal to do with the relapses of typhoid fever. So in malaria; if I succeed in reducing the size of the spleen within a reasonable time I feel sure that the malaria is under control, but in fever districts in the South as in the North, in the swamps, there are cases that will not easily get well. There are also those very obstinate cases in which the spleen grows very slowly for weeks and months, until finally cachexia is the first, and the "chill and fever" only the second, symptom. These cases are very apt to resist the influence of quinin. The practice Dr. Didama speaks of, of giving calomel before giving quinin, and getting the stomach in good order, is a very good one, mainly in these old cases. There are those in which quinin will not act until the stomach is put in good condition for absorption, by a purgative or otherwise; sometimes by an emetic or irrigation of the stomach, always by stomachics.

Regarding the preparations that I have used, I can say that I have not given a single sugar-coated pill for thirty years. I seldom prescribe drugs even in capsules, because I know capsules may pass through the intestinal tract. I generally use powders in preference to anything else because I feel tolerably sure the quinin will then act. I order solutions only for those who do not mind the taste.

To-day I simply state to you my observations made during forty years or more, that there are cases of malaria which, after not getting well with quinin or with arsenic, do gradually get well with ergot. Now, there is no reasoning against that. If you always cure your patients with quinin only so much the better for you. I did not always succeed. In my failures I often succeeded with ergot. If some one does not see why that should be so I cannot to-

day disperse his doubts. It is not the first time nor the last that empiric facts have collided with our insufficient information, and that theoretic reasons would come limping behind actual observation. I have tried to suggest the way in which ergot may prove effective in malaria; maybe a better interpretation of its action may be found. I believe I am on perfectly safe ground when I display my clinical observations, which, as I said, extend over forty years.

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